

**REMARKS**

Claims 1-47 are all the claims pending in the application; claims 14 and 31-39 are withdrawn from consideration; claims 1-13, 15-30 and 40-47 are rejected.

Claim 1 has been amended to more clearly state that which the Applicants regard as their invention. Applicants have amended claim 1 to recite that the combination of amino acids corresponding to  $R^1$  and  $R^2$  may be between 0 and 15 amino acids. Support for this amendment can be found in the specification at page 10, lines 27-28, where it is stated that  $R^1$ - $R^2$  is a number of amino acids ranging from 0-15 for the combination  $R^1$ - $R^2$ .

Applicants have also amended claim 1 to explicitly state  $R^3$  is between 0 and 15 amino acids (supported in the specification at page 10, lines 27-28), rather than " $\geq 0$ ".

Claim 1 has also been amended to incorporate the fact that the motif "(A-B-C-A)" may be present in formula (I) in the reverse orientation.

Claims 3 and 4 have been amended to revise symbols used in the claims.

Claims 8-12 have been amended to more clearly recite the invention.

Claim 15 has been amended to remove reference to the use for the composition recited in the claim.

New claims 48-50 are fully supported by the specification. Claim 48 recites subject matter originally recited in claim 4. This amendment was made to correct an obvious error. Claim 4 recited a group of specific residues that may be represented by  $R^1$ , i.e., ACAA, Gly<sub>p</sub> and Ala<sub>q</sub>. However, as set forth at page 11, lines 2-3, the ACAA group applies to  $R^2$  rather than  $R^1$ . Thus, claim 4 has been amended to cancel reference to ACAA, and a new claim 48 has been added that recites  $R^2$  as being ACAA.

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Support for claims 49 and 50 may be found at page 21, line 23, through page 22, line 21.

Thus, no new matter has been added and entry of this amendment is earnestly solicited.

**I. Rejection of claims under 35 U.S.C. §101**

At page 4 of the Office Action, paragraph 7, claims 8-12 are rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter.

The Examiner asserts that the claims do not explicitly indicate that hand of man and suggests that the term “purified” be inserted.

In response, Applicants assert that the peptides recited in the rejected claims are synthetic peptides, i.e., not derived from an organism. Under U.S. practice, the term “purified” is only used to refer to naturally-occurring proteins. Thus, the Examiner’s position is without merit and Applicants respectfully request reconsideration and withdrawal of this rejection.

**II. Rejection of claims under 35 U.S.C. §112**

A. At page 5 of the Office Action, paragraph 8, claims 1-13, 15-30 and 40-47 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner asserts that (i) formula (I) is not reflected in the written part of claim 1 describing the formula, (ii) the dependent claims are not consistent with the formula, and (iii) the comparison of the amino acids sequence of BP1, BP2, BP2.3, BP2.4 and BP2.5 with formula (I) shows that these sequences do not conform to formula (I).

(i) As to point (i), the Examiner states that it appears that the parenthetical (A-B-C-A) can be repeated, or put into reverse orientation, and that the individual amino acids in the repeats can differ between repeats. However, the Examiner states, such is not apparent from the wording of the claim and the structure of formula (I).

In response, Applicants have amended formula (I) to more clearly recite that the motif (A-B-C-A) may be present in either of two orientations (i.e., A-B-C-A or A-C-B-A). Thus, formula (I) now fully reflects have the motif in either of two orientations.

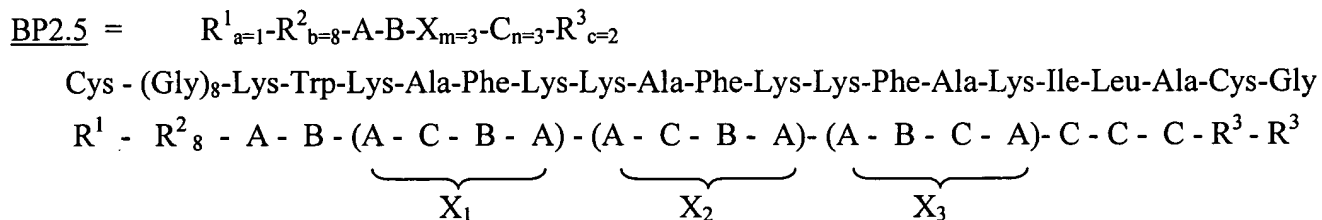
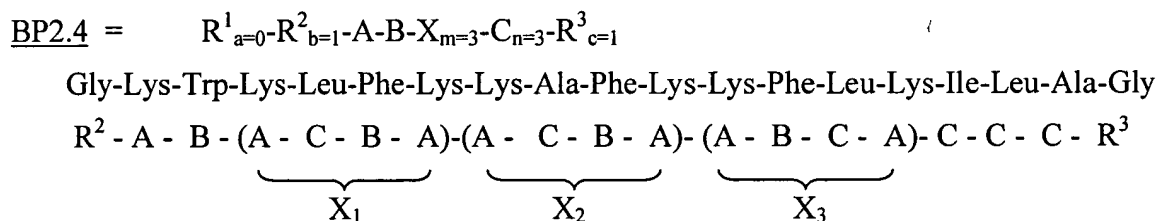
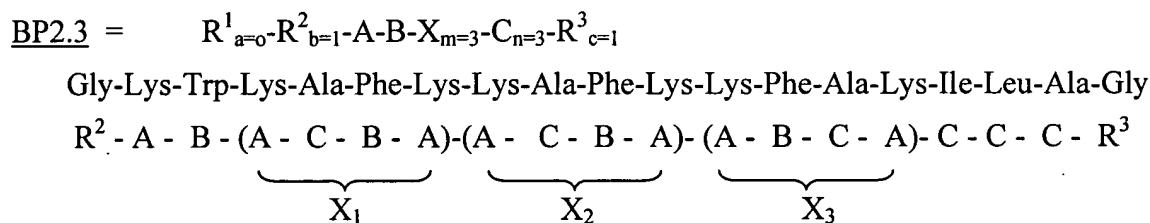
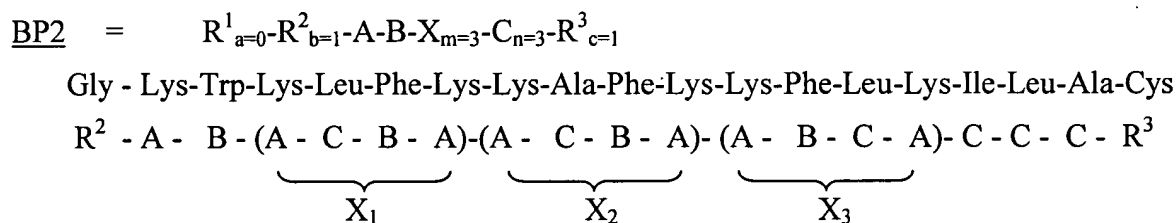
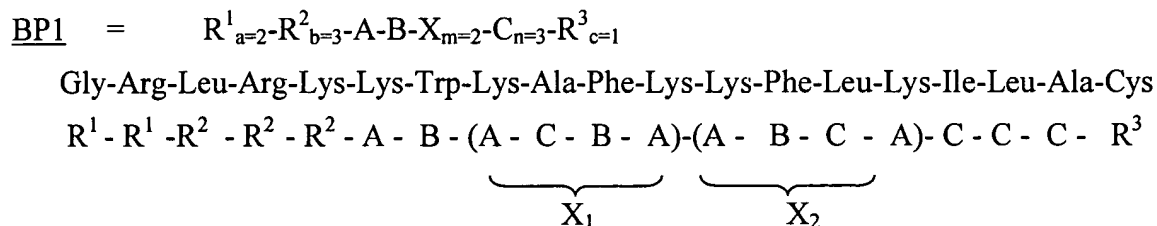
(ii) Based on the amino acid sequence of the five peptides the Examiner sets forth in the Office Action (BP1, BP2, BP2.3, BP2.4 and BP2.5), the Examiner concludes that the dependent claims are not consistent with formula (I). In particular, the Examiner notes that while R<sup>1</sup> is said to be "an amino acid" (i.e., one amino acid), claim 4 permits R<sup>1</sup> to be as many as 10 amino acids.

In response, Applicants have amended claim 1 to recite that R<sup>1</sup> may be between 0 and 15 amino acids. As described above, support for this amendment can be found in the specification at page 10, lines 27-28, where it is stated that the combination of R<sup>1</sup> and R<sup>2</sup> is a number of amino acids ranging from 0-15.

Thus, the claim 4 is now consistent with the number of amino acids recited for R<sup>1</sup> in claim 1.

(iii) The Examiner asserts that the five peptides represented by BP1, BP2, BP2.3, BP2.4 and BP2.5 do not fall within formula (I).

In light of the clarifying amendments to claim 1, Applicants assert that each of the peptides cited by the Examiner falls within formula (I). Applicants provide the following comparison for each of the five peptides for the Examiner's convenience.



B. At page 7 of the Office Action, paragraph 9, claims 1-7, 13, 15-30 and 40-47 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner states that the use of the terms “R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> each are an amino acid, x is an integer  $\geq 0$ , y is an integer  $\geq 0$ ” and “may have the retrograde orientation (A-C-B-A)” render the claim indefinite.

As to the former term, the Examiner contends that claim 1 does not clearly indicate which amino acids are used for R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> and how many R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are included in the peptide. In response, Applicants assert that the claims are not limited, in that the specification defines the amino acids represented by R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> as being any amino acid, of any number, as set forth at page 12, lines 1-8. Thus, in contrast to the Examiner’s position, the claims are definite as written.

However, in order to further the prosecution of the application, Applicants have amended claim 1 to recite that R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> may each be between 0 and 15 amino acids (and that the combination of R<sup>1</sup> and R<sup>2</sup> cannot total more than 15 amino acids), thus providing an upper limit to the number of amino acids represented by each element.

As to the latter term, Applicants have amended claim 1 to include the possibility of having the motif (A-B-C-A) in reverse orientation in formula (I).

C. At page 7 of the Office Action, paragraph 10, claim 4 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner states that claim 4 recites the limitation “ACAA, ...Gly<sub>p</sub>, ....Ala<sub>q</sub>....” in lines 3-5. The Examiner states that there is insufficient antecedent basis for the limitation in the claim.

In response, in view of the amendment to claim 1 to recite that  $R^1$  may be between 0 and 15 amino acids, Applicants assert that there is adequate antecedent basis in claim 4 for the limitation cited by the Examiner.

Applicants have also amended claim 4 to correct an obvious error. As it is now recited, claim 4 recites a group of specific residues that may be represented by  $R^1$ , i.e., ACAA, Gly<sub>p</sub> and Ala<sub>q</sub>. However, as set forth at page 11, lines 2-3, it appears that the ACAA group applies to  $R^2$  rather than  $R^1$ . Thus, claim 4 has been amended to cancel reference to ACAA, and a new claim (claim 48) has been added that recites  $R^2$  as being ACAA.

D. At page 7 of the Office Action, paragraph 11, claim 6 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner contends that the use of the term “in a greater amount than” renders the term indefinite as it is unclear how many more motifs of (A-C-B-A) than (A-B-C-A) are present.

In response, Applicants assert that the claim is clear as written, i.e., the appearance of the motif (A-C-B-A) occurs more often than the appearance of the motif (A-B-C-A). As recited in claim 1, the number of motifs represented by X (i.e., A-B-C-A or A-C-B-A) is between 2 and 8 (m is an integer between 2 and 8). As a result, there must be at least 2 copies of the motif A-C-B-A (if there was one of each, the “greater amount” limitation would not be met). Further, the maximum number of copies of the motif A-C-B-A would be 8 (with a corresponding absence of any of the motif A-B-C-A). The skilled artisan would understand that the scope of claim 6 is thus limited to the following possibilities:

<u>Number of motif A-C-B-A present</u>	<u>Corresponding possible number of motif A-B-C-A present</u>
2	0-1
3	0-2
4	0-3
5	0-3
6	0-2
7	0-1
8	0

Thus, there are 19 different peptides encompassed within the scope of claim 6.

Applicants therefore assert that the claim is definite as written.

E. At page 8 of the Office Action, paragraph 12, claims 8-12 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner interprets the term “having”, as used in these claims as “comprising” and objects to the open-ended nature of the term.

In response, Applicants have been amended to replace the term “having” with the term “comprising.” Support for the additional substituents that may be included with the peptide may be found at page 4, lines 30-31; page 11, line 10; and page 11, line 21 through page 12, line 8.

F. At page 8 of the Office Action, paragraph 13, claims 15, 24, 25 and 41 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner contends that the cited claims are indefinite because each recites a pharmaceutical composition comprising the same ingredients. The Examiner explains that the treatment of a specific disease state is an intended use which does not provide any weight in the claims.

In response, Applicants have cancelled claims 24, 25 and 41. Applicants have also amended claim 15 to recite a pharmaceutical composition, as well as added new claims to recite

a composition comprising the peptide of the invention in an amount effective for the treatment of several conditions (claim 49), and the different formulations of the composition (claim 50).

Support in the specification for the different formulations may be found at page 5, lines 16-28; page 13, lines 16-17; page 21, lines 27-28; page 20, line 24 through page 21, line 22; and page 13, lines 16-19.

In view of each of these points, and the amendments to the claims, Applicants respectfully request reconsideration and withdrawal of each of the rejections under 35 U.S.C. §112.

### **III. Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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**APPENDIX**  
**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE CLAIMS:**

**Claims 2, 24, 25 and 41 are canceled.**

**The claims are amended as follows:**

1. (Twice Amended) A purified peptide comprising at least 12 amino acids, the peptide having an amino acid composition such that the peptide is amphipathic, cationic and forms a stable  $\alpha$ -helix and is represented by the following formula (I) or the retro orientation of formula (I):



wherein

$R^1$ ,  $R^2$ , and  $R^3$  are each an amino acid and may be the same or different,

a is an integer from 0 to 15,

b is an integer from 0 to 15,

wherein the combination of a + b is not greater than 15,

x is an integer from  $\geq 0$  to 15,

cy is an integer from  $\geq 0$  to 15,

each A is an amino acid independently selected from the group consisting of Lys, Arg and His,

each B is an amino acid independently selected from the group consisting of Phe, Trp and Tyr,

each C is an amino acid independently selected from the group consisting of Leu, Ile, Val and Ala,

X is either (A-B-C-A) or (A-C-B-A).

m is an integer of from 2 to 8, and

n is an integer of from 1 to 3, and

~~wherein one or more of the sequence motifs (A-B-C-A) may have the retro-orientation~~  
(A-C-B-A).

3. (Amended) The purified peptide according to claim 1, wherein a + b and c ~~x and y~~ are each an integer of from 1 to 10.

4. (Twice amended) The purified peptide according to claim 1, wherein  $R_a^1$  is selected from the group consisting of:

~~ACAA, wherein each A and C is as independently defined in claim 1;~~

Gly<sub>p</sub>, wherein p is an integer of from 1 to 10; and

Ala<sub>q</sub>, wherein q is an integer of from 1 to 10.1

8. (Thrice amended) A The peptide BP 1, comprising amino acids 1 to 19 of having  
SEQ ID NO: 1.

9. (Thrice amended) A The peptide BP 2, comprising amino acids 1 to 19 of having  
SEQ ID NO: 2.

10. (Thrice amended) A The peptide BP 2.3, comprising amino acids 1 to 19 of  
~~having~~ SEQ ID NO: 3.

11. (Thrice amended) A The peptide BP 2.4, comprising amino acids 1 to 19 of  
~~having~~ SEQ ID NO: 4.

12. (Thrice amended) A The-peptide BP-2.5, comprising amino acids 1 to 29 of  
~~having~~ SEQ ID NO: 5.

15. (Twice amended) A pharmaceutical composition comprising a peptide according  
to claim 1 as an active component ~~for treating topical and systemic microbial or parasite~~  
~~infection, or both,~~ and a pharmaceutically acceptable carrier in a pharmaceutically acceptable  
dosage form.

**Claims 48-50 are added as new claims.**